510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE

A. 510(k) Number:

k043218

B. Purpose for Submission:

Additional features added to previously marketed device

C. Measurand:

The ABL800 FLEX with FLEXQ Module is intended for in vitro testing of samples of whole blood for the parameters pH, pO_2, pCO_2, potassium, sodium, calcium, chloride, glucose, lactate, total bilirubin, and co-oximetry parameters (total hemoglobin, oxygen saturation, and the hemoglobin fractions FO_2Hb, FCOHb, FHHb and FHbF) as well as for in vitro testing of samples of expired air for the parameters PO_2 and PCO_2.

D. Type of Test:

With respect to sensor technology, the ABL800 FLEX is substantially equivalent to the predicate device ABL700 Series upgrade

	ABL800 FLEX Sensor Technology	ABL700 Series Upgrade Sensor Technology
Blood gases and pH	Electrochemical	Electrochemical
Sodium	Electrochemical	Electrochemical
Potassium	Electrochemical	Electrochemical
Calcium	Electrochemical	Electrochemical
Glucose	Electrochemical	Electrochemical
Lactate	Electrochemical	Electrochemical
Co-oximetry parameters	Optical	Optical
Bilirubin	Optical	Optical

E. Applicant:

Radiometer Medical ApS

F. Proprietary and Established Names:

ABL800 FLEX with FLEXQ Module

G. Regulatory Information:

Regulation section:

	CFR Section	Device Class	Product Code
Blood gases and blood pH	862.1120	II	CHL
Sodium test system	862.1665	II	JGS
Potassium test system	862.1600	II	CEM
Calcium test system	862.1145	II	JFP
Chloride test system	862.1170	II	CGZ
Glucose test system	862.1345	II	CGA
Lactic acid test system	862.1450	I	KHP
Bilirubin (total or direct test system	862.1110	II	CIG
Bilirubin in the neonate test system	862.1113	I	MQM
Carboxyhemoglobin assay	864.7425	II	GHS
Automated hemoglobin system	864.5620	II	GKR
Fetal hemoglobin assay	864.7455	II	KQI

H. Intended Use:

1. Intended use(s):

   See Indication(s) for use below.

2. Indication(s) for use:

   The ABL800 FLEX with FLEXQ Module is intended for in vitro testing of samples of whole blood for the parameters pH, pO_2, pCO_2, potassium, sodium, calcium, chloride, glucose, lactate, total bilirubin, and co-oximetry parameters (total hemoglobin, oxygen saturation, and the hemoglobin fractions FO_2Hb, FCOHb, FMetHb, FHHb and FHbF) as well as for in vitro testing of samples of expired air for the parameters PO_2 and PCO_2.

   Indications for use information for the analytes measured by the ABL800 FLEX:

   pH: pH is the indispensable measure of academia or alkalemia and is therefore an essential part of the pH/blood gas measurement. The normal function of many metabolic processes requires a pH to be within a relatively narrow range.

   pO_2: The arterial oxygen tension is an indicator of the oxygen uptake in the lungs.

   pCO_2: pCO_2 is a direct reflection of the adequacy of alveolar ventilation in relation to the metabolic rate.

   Potassium (*c*K+): The measurements of the concentration of potassium ions in plasma are used to monitor the electrolyte balance.

   Sodium (*c*Na+): The measurements of the concentration of sodium ions in plasma are used to monitor the electrolyte balance.

Calcium (*c*Ca_2+): The measurements of the concentration of calcium ions in plasma are used to monitor the electrolyte balance.

Chloride (*c*Cl^-): The measurements of the concentration of chloride ions in plasma are used to monitor the electrolyte balance.

Glucose (*c*Glu): The glucose measurements measure the concentration of glucose in plasma. The glucose measurements are used to screen for, diagnose and monitor diabetes, pre-diabetes, and hyper- and hypoglycemia.

Lactate (*c*Lac): The lactate measurements measure the concentration of lactate in plasma. Lactate measurements serve as a marker of critical imbalance between tissue oxygen demand and oxygen supply.

Bilirubin (*c*tBil): the bilirubin measurements measure the total concentration of bilirubin in plasma, *c*t Bil is used to assess the risk of hyperbilirubinemia.

Total Hemoglobin (*c*tHb): *c*tHb is a measure of the potential oxygen-carrying capacity of the blood.

Oxygen Saturation (*s*O_2): *s*O_2 is the percentage of oxygenated hemoglobin in relation to the amount of hemoglobin capable of carrying oxygen. *s*O_2 allows evaluation of oxygenation.

Fraction of Oxyhemoglobin (*F*O_2Hb): *F*O_2Hb is a measure of the utilization of the potential oxygen transport capacity; that is the fraction of oxyhemoglobin in relation to all hemoglobins present (*t*Hb) including dyshemoglobins.

Fraction of Carboxyhemoglobin (is the fraction of carboxyhemoglobin. It is incapable of transporting oxygen.

Fraction of Methemoglobin (*F*MetHb): *F*MetHb is the fraction of methemoglobin. It is incapable of transporting oxygen.

Fraction of Deoxyhemoglobin in Total Hemoglobin (*F*HHb): *F*HHb is the fraction of deoxyhemoglobin in total hemoglobin. It can bind oxygen then forming oxyhemoglobin.

Fraction of Fetal Hemoglobin (*F*HbF): Fetal hemoglobin consists of two α-chains and two β-chains, and has a higher oxygen affinity than adult Hb.

3. Special conditions for use statement(s):

For Prescription Use

4. Special instrument requirements:

   ABL800 FLEX Blood Gas Analyzer with FLEXQ module.

I. Device Description:

The ABL800 FLEX with FLEXQ Module is an ABL800 FLEX Analyzer with the added optional capability of automatic sampling of up to three blood samples. The analyzer part of the ABL800 FLEX with FLEXQ is identical to the analyzer part of the ABL800 FLEX. The ABL800 FLEX, the ABL800 FLEX with FLEXQ Module consists of several modules of the same analyzer for the measurement of blood gas, electrolyte, metabolite and co-oximetry.

The FLEXQ Module is designed to work with the vented arterial blood sampler, *safe* PICO (k043143) the *safe* PICO consists of a graduated plastic sample barrel coded with a unique barcode and a plunger. Within the sampler barrel is a soft, coated magnetic steel ball for mixing the sample before measurement and dry electrolyte-balanced lithium/sodium heparin. The sampler includes a vented tip cap that allows the sampler to be vented after the appliance of the tip cap to the male connector of the sampler. The *safe*PICO may be delivered with a conventional PVC needle cube or with a transparent plastic needle shield device connected to the needle. The needle shield consists of two axially aligned plastic tubes, each with a slit where a tab from the other may slide. Activating the thumb grip on the inner tube causes the inner tube to slide along inside the outer tube and to cover the needle point by at least 8 mm.

Installing the FLEXQ module into an existing ABL800 FLEX Analyzer includes physically installing the module and loading upgraded software, which controls the functions of the FLEXQ module. The FLEXQ module comprises a sampler tray with three slots for holding up to three samplers simultaneously. Each slot has an optical switch detecting the presence of a sampler. The FLEXQ module has a barcode reader, which can read out the barcode of the samplers. The FLEXQ module includes a rotating magnet system located under the sampler tray, which interacts with the steel ball in the sampler barrel and automatically mixes the sample prior to measuring.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   The ABL800 FLEX with FLEXQ Module is substantially equivalent in features and characteristics to the predicate devices ABL800 FLEX (k041874) manufactured by Radiometer Medical ApS and AVL 9181 Electrolyte Analyzer (k972673) manufactured by AVL Scientific Corporation.

2. Predicate 510(k) number(s):

   k041874
   k972673

3. Comparison with predicate:

   See method comparison with predicate device below.

K. Standard/Guidance Document Referenced (if applicable):

Electrical Safety and EMC

Approvals: UL, CSA. In compliance with IEC 61010-1. Installation category II

EMC Emission: The equipment complies with the emission requirements for Class B equipment in EN 61326-1: Electrical equipment for measurement, control and laboratory use – EMC requirements part 1: General requirements.

EMC Immunity: The equipment complies with immunity requirements in EN 61326-1: Electrical equipment for measurement, control and laboratory use – EMC requirements part 1: General requirements.

L. Test Principle:

Potentiometric measuring principle
The potential of an electrode chain is recorded using a voltmeter, and related to the concentration of the sample (the Nernst equation).

An electrode chain describes an electrical circuit consisting of a sample, electrode, reference electrode, voltmeter, membranes, and electrolyte solutions. Every element in the electrode chain contributes a voltage to the total potential drop through the chain. Thus:

- When immersed in the appropriate electrolyte solution, both electrodes have separate potentials.
- The membrane junctions between the sample and electrolyte solutions also have separate potentials.

The potentiometric measuring principle is applied to pH, pCO_2, and electrolyte electrodes.

Amperometric measuring principle
The magnitude of an electrical current flowing through an electrode chain, which is in turn proportional to the concentration of the substance being oxidized or reduced at an electrode in the chain.

The electrode chain in amperometric measurements consists of the sample, the two electrodes (anode and cathode), an amperemeter, a voltage source, the membrane, and the electrolyte solution.

To simplify the description of the measuring process in an amperometric electrode, we make the following assumptions:

- There is a species **A** in the sample which is reduced at the cathode to $\mathbf{A}^-$.
- There is a species **X** in the electrolyte which is oxidized at the anode to $\mathbf{X}^+$.

The membrane is selective to the species **A**, allowing no other species but it to pass through from the sample into the electrolyte solution.

As appropriate potential is applied across the electrodes, the species **A** is reduced as the cathode according to the following reaction:

$$A + e^- \rightarrow A^-$$

The reduction of **A** produces a flow of electrons, i.e. an electrical current.

To complete the electrical circuit an oxidation reaction where electrons are released is necessary. Therefore species **X** is oxidized according to the following reaction:

$$X \rightarrow X^+ + e^-$$

The magnitude of the current flowing through the circuit is proportional to the concentration of the species being reduced, in this case species **A**. The analyzer thereby automatically calculates the concentration on **A** in the sample.

The amperometric measuring principle is applied in the pO_2, glucose, and lactate electrodes.

Optical measuring principles

The optical system of the ABL800 FLEX analyzer is designed to measure the following parameters:

Parameter	**Description**
ctHb	concentration o f total hemoglobin
sO_2	oxygen saturation
FO_2Hb	fraction of oxyhemoglobin
FCOHb	fractionation of carboxyhemoglobin
FHHb	fractionation of deoxyhemoglobin
FMetHb	fraction of methemoglobin
FHbF	fraction of fetal hemoglobin
ctBil	concentration of total bilirubin (the sum of conjugated and conjugated bilirubin) in plasma

Note: ctBil can be measured on a whole blood or plasma sample. Plasma samples provide the optimal measurement performance. To obtain optimal accuracy when following a patient trend in ctBil, use the same aspiration mode and same analyzer.

Hematocrit (Hct) is also available as a derived parameter.

The optical system is based on a 128-wavelength spectrophotometer with a measuring range of 478-672 nm. The spectrophotometer is connected via an optical fiber to a combined hemolyzer and measuring chamber.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:
   a. Precision/Reproducibility:

The precision (i.e. repeatability or within-run imprecision) and reproducibility (i.e. total imprecision) results for the parameters as well as the linearity/assay reportable ranges were established from a single large-sized study.

The variation parameters of the study appears from the table below

Parameter	**(n)**
Observations	2
Days	11
Instruments	11
Operators	3
Sites	1
Runs	16

The study was performed as a large comparative in-house study using 11 ABL8xx FLEX analyzers and 5 ABL735 analyzers. The study used the average of the 5 ABL735 analyzers (adjusted for drift of the parameters in the sample) as reference values. The study was designed to comprise all measuring modes of all the configurations of the ABL8xx FLEX analyzer on all parameters. All measurements on the ABL8xx FLEX analyzers were made as doubles. Three in-house operators located at one site performed the measurements during 11 working days - from March 22, 2004 to April 6, 2004.

Below are listed tables showing the %CV for the parameters of the ABL800 FLEX analyzer:

pH	**CV-Micromode**	**CV-Macromode**
	%	%
6.80	0.121	0.089
6.90	0.115	0.083
7.00	0.111	0.081
7.10	0.110	0.080
7.20	0.109	0.082
7.25	0.110	0.083
7.30	0.111	0.085
7.40	0.115	0.091
7.50	0.123	0.101
7.60	0.133	0.112

pCO_2	CV-Micromode	CV-Macromode
mmHg	%	%
15.00	4.719	2.979
17.00	4.655	2.894
19.99	4.591	2.809
39.96	4.500	2.643
59.98	4.551	2.642
80.00	4.630	2.679
119.94	4.828	2.831
140.05	4.956	2.960
149.90	5.028	3.042
159.97	5.111	3.140

pO_2	CV-Macromode	CV-Micromode
mmHg	%	%
14	1.866	4.018
15	1.848	4.005
20	1.796	3.958
25	1.771	3.929
35	1.750	3.899
45	1.743	3.897
50	1.741	3.904
65	1.742	3.961
75	1.745	4.025
80	1.748	4.064
85	1.368	3.406
120	1.360	3.343
150	1.356	3.305
180	1.354	3.281
210	1.354	3.273
250	1.356	3.285
280	1.361	3.312
310	1.367	3.354
340	1.375	3.409
390	1.393	3.532
410	1.816	4.675
420	1.799	4.576
430	1.783	4.484
440	1.769	4.401
450	1.757	4.325
460	1.747	4.259
480	1.732	4.153
510	1.724	4.069
530	1.730	4.066
550	1.742	4.104

$c\mathrm{K}^+$	CV-Micromode	CV-Macromode
mmol/L	%	%
1.65	4.294	4.009
2.01	3.672	3.330
2.46	3.190	2.784
3.00	2.824	2.348
3.32	2.677	2.165
3.67	2.551	2.004
4.48	2.365	1.752
5.47	2.241	1.569
6.69	2.156	1.432
8.17	2.102	1.334

$c\mathrm{Na}^+$	CV-Micromode	CV-Macromode
mmol/L	%	%
119.10	1.210	0.926
127.74	1.188	0.897
134.29	1.174	0.879
141.17	1.165	0.868
148.41	1.170	0.874
156.02	1.175	0.881
164.02	1.180	0.888
172.43	1.187	0.897
181.27	1.194	0.907
200.34	1.211	0.931

$c\mathrm{Ca}^{2+}$	CV-Micromode	CV-Macromode
Mmol/L	%	%
0.50	8.778	3.771
0.75	5.865	2.550
0.95	4.641	2.039
1.15	3.843	1.707
1.35	3.284	1.476
1.55	2.870	1.307
1.75	2.553	1.178
1.95	2.301	1.078
2.10	2.145	1.017
2.21	2.045	0.979

$c\mathrm{Cl}^-$	CV-Micromode	CV-Macromode
Mmol/L	%	%
85.63	0.273	1.344
94.63	0.241	1.346
99.48	0.239	1.351
104.58	0.239	1.358
109.95	0.239	1.368
115.58	0.242	1.381
121.51	0.246	1.396
127.74	0.254	1.416
134.29	0.267	1.439
149.90	0.309	1.504

*c*Glu	CV-Micromode	CV-Macromode
Mmol/L	%	%
0.49	23.172	21.768
1.00	13.610	12.469
2.25	8.042	7.203
4.00	5.806	5.161
6.25	4.624	4.113
7.84	4.153	3.706
9.00	3.902	3.490
10.24	3.689	3.309
12.25	3.422	3.085
15.21	3.143	2.854

*c*Lac	CV-Micromode	CV-Macromode
Mmol/L	%	%
0.15	35.878	34.841
0.37	18.083	15.707
1.00	13.181	9.233
2.72	12.899	8.329
4.48	13.143	8.450
5.75	13.297	8.563
7.39	13.463	8.697
9.49	13.639	8.848
12.18	13.824	9.015
15.64	14.016	9.196

***c*tHb**	**CV-Micromode**	**CV-Macromode**
Mmol/L	%	%
2.00	3.297	2.241
4.00	3.293	2.224
6.00	3.290	2.211
8.00	3.288	2.201
10.00	3.287	2.193
12.00	3.286	2.188
14.00	3.286	2.187
17.00	3.287	2.190
20.00	3.290	2.200
24.00	3.295	2.223

b. Linearity/assay reportable range:

The protocol used for the test of linearity is an integrated part of the experimental design for performance testing. The experimental design is basically a randomized experiment, where the measurements in the different modes of the analyzer are performed in a randomized sequence for each of the blood preparations.
Bias is defined as:

$$Bias_{Ref} = X_{ABL800Flex} - X_{Primary\ Reference\ method}$$
$$Bias_{ABL} = X_{ABL800Flex} - X_{ABL735}$$

Where

$X_{ABL800Flex}$ is the mean value of the measured value for a group of ABL800Flex analyzer.
$X_{Primary\ Reference\ method}$ is the mean value of the measured value obtained with the Primary Reference method.
X_{ABL735} is the mean value of the measured value for the ABL735 analyzers used as reference analyzers.

The acceptance criteria for linearity are the maximum bias values, specified at different values of the particular parameter. These values are chosen to cover the entire test range.
The maximum bias values were specified in the design specifications for the analyzer. Requirements for the maximum bias values assure that the linearity is within acceptance criteria. The maximum bias values specified in the design specifications for the ABL800 series analyzers are given in Tables 1 and 2. The actual measured bias values from the data of the verification test are also presented in Tables 1 and 2.
From the Tables 1 and 2 it is seen that all acceptance criteria for bias, and thereby also for linearity, are met. The concept of using bias requirements for test of linearity is illustrated in Figure 1 below.

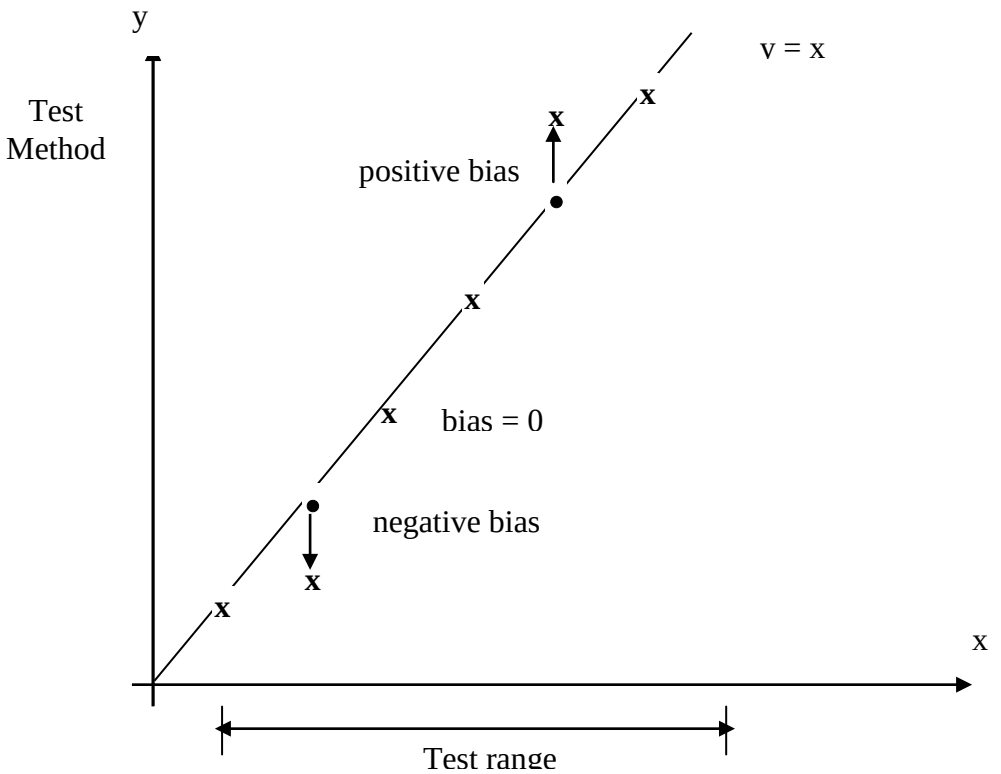

Fig. 1

Micromode

Parameter	Level	Unit	95% Confidence Intervals (in specified units)			Accepted/ not accepted
			Lower Limit	Upper Limit	Acceptance criteria	
pH	7.0		-0.009	0.006	±0.01	accepted
pH	7.4		0.003	0.005	±0.005	accepted
pH	7.6		-0.008	0.006	±0.01	accepted
pO2	15	mmHg	-0.81	0.04	±2	accepted
pO2	50	mmHg	-0.39	1.71	±2	accepted
pO2	150	mmHg	-2.17	3.38	±4	accepted
pO2	250	mmHg	-5.32	2.68	±6	accepted
pO2	530	mmHg	-39.09	17.09	±40	accepted
pCO2	15	mmHg	-0.79	0.38	±0.8	accepted
pCO2	40	mmHg	-0.87	0.61	±1	accepted
pCO2	60	mmHg	-0.42	2.28	±3	accepted
pCO2	80	mmHg	-1.25	2.99	±3	accepted
pCO2	150	mmHg	-3.15	9.90	±10	accepted
Cl	85	mmol/L	0.15	1.00	±3.5	accepted

Cl	105	mmol/L	1.66	2.50	±3.0	accepted
Cl	140	mmol/L	2.81	1.83	±3.0	accepted
Ca	0.5	mmol/L	0.03	0.08	±0.08	accepted
Ca	1.25	mmol/L	0.03	0.06	±0.06	accepted
K	2	mmol/L	-0.07	-0.02	±0.08	accepted
K	4	mmol/L	0.20	0.24	±0.25	accepted
K	8	mmol/L	0.28	0.43	±0.45	accepted
Na	120	mmol/L	0.24	1.44	±1.5	accepted
Na	140	mmol/L	1.10	0.12	±1.5	accepted
Na	180	mmol/L	1.12	0.22	±1.5	accepted
Glu	2	mmol/L	-0.07	0.04	±0.1	accepted
Glu	5	mmol/L	-0.09	0.15	±0.2	accepted
Glu	15	mmol/L	-0.26	0.49	±0.6	accepted
Lac	0.3	mmol/L	-0.02	0.08	±0.1	accepted
Lac	2	mmol/L	0.06	0.27	±0.3	accepted
Lac	10	mmol/L	-0.30	-1.05	±1.1	accepted
tHb	7	g/dL	0.28	-0.12	±0.3	accepted
tHb	15	g/dL	0.54	0.12	±0.6	accepted
tHb	25	g/dL	1.40	0.05	±1.5	accepted

Table 1

Macromode

Parameter	Level	Unit	95% Confidence Intervals (in specified units)			Accepted/ not accepted
			Lower limit	Upper limit	Acceptance criteria	
pH	7.0		-0.005	-0.002	±0.005	accepted
pH	7.4		-0.003	-0.001	±0.005	accepted
pH	7.6		-0.005	0.000	±0.005	accepted
pO2	15	mmHg	-0.03	0.12	±1.5	accepted
pO2	50	mmHg	0.34	0.61	±1.5	accepted
pO2	150	mmHg	-1.87	-0.97	±2	accepted
pO2	250	mmHg	-2.57	-0.57	±3	accepted
pO2	530	mmHg	-12.59	-6.23	±15	accepted
pCO2	15	mmHg	-0.49	-0.30	±0.5	accepted
pCO2	40	mmHg	-0.59	-0.03	±0.6	accepted
pCO2	60	mmHg	-0.12	1.02	±1.1	accepted
pCO2	80	mmHg	-1.05	0.83	±1.5	accepted
pCO2	150	mmHg	-0.75	4.28	±6	accepted
Cl	85	mmol/L	0.15	1.34	±3.5	accepted
Cl	105	mmol/L	1.66	2.81	±3	accepted
Cl	140	mmol/L	1.41	2.95	±3	accepted
Ca	0.5	mmol/L	0.03	0.05	±0.05	accepted
Ca	1.25	mmol/L	0.01	0.03	±0.03	accepted
K	2	mmol/L	-0.04	-0.01	±0.07	accepted
K	4	mmol/L	0.19	0.23	±0.25	accepted
K	8	mmol/L	0.18	0.32	±0.4	accepted
Na	120	mmol/L	-0.36	1.08	±1.1	accepted
Na	140	mmol/L	-0.44	0.75	±0.8	accepted
Na	180	mmol/L	-0.05	0.58	±1	accepted
Glu	2	mmol/L	-0.04	0.00	±0.1	accepted
Glu	5	mmol/L	0.00	0.10	±0.12	accepted
Glu	15	mmol/L	0.07	0.43	±0.5	accepted
Lac	0.3	mmol/L	-0.03	0.01	±0.1	accepted
Lac	2	mmol/L	-0.07	0.11	±0.12	accepted
Lac	10	mmol/L	-0.80	0.20	±0.9	accepted
tHb	7	g/dL	-0.01	0.11	±0.3	accepted
tHb	15	g/dL	0.29	0.44	±0.5	accepted
tHb	25	g/dL	0.90	1.23	±1.3	accepted

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

pH
Capillary-type glass pH electrode with a saturated calomel reference electrode and a liquid junction saturated with KCL (BMS™ Mk2) [1, 2].

pCO_2
Tonometry [3].
The gas used for tonometry is traceable to NIST certified Standard Reference Materials.

pO_2
Tonometry [3].
The gases used for tonometry are traceable to NIST certified Standard Reference Materials.

K^+
NIST certified Standard Reference Material SRM 909b (human serum).

Na^+
NIST certified Standard Reference Material SRM 909b (human serum) and Radiometer specified standard serum material (specified using flame photometry).

Cl^-
NIST certified Standard Reference Material SRM 909b (human serum)

Ca^{2+}
The calcium transfer standards were used. These are traceable to NIST SRM915 and have an ionic strength of 160.0 mmol per kg of water and pH 7.40 at 37 °C, using 1 mmol/L (37 °C) HEPES buffer. The standards were produced as indicated in [4].

Glu
Spectrophotometry, using the hexokinase (HK) method recommended by NCCLS [5], measured on serum.

Lac
Spectrophotometry using lactate dehydrogenase (LDH) method, measured on serum [10].

Hb
HiCN method recommended by NCCLS [6].

Oximetry
The optical system is unchanged in the ABL800 FLEX analyzers compared to the ABL700 Series. Tests of ctHb on the ABL800 FLEX analyzer have been conducted. As the other oximetry parameters (sO_2, FO_2Hb, FCOHb, FMetHb, FHHB, FHbF) are derived from ctHb, these parameters have not been re-tested; the information and results below are from the ABL700 Series.

The reference method established for the oximetry parameters used modified ABL520 analyzers

as the reference instruments. The ABL520 analyzers have been validated and their performance specifications determined according to primary reference methods.

The modified ABL520 analyzers are used in accordance with IFCC's recommendations for traceability of reference methods.

References

List of references

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8. Kristoffersen K. An improved method for the estimation of small quantities of alkali-resistant hemoglobin in blood. Scand J Clin Lab Invest 1961; 13: 402.

9. Quantitative measurement of fetal hemoglobin using the alkali denaturation method. Approved Guideline. NCCLS Publication H13-A 1989; 9, 18.

10. Begmeyer. Methods of enzymatic analysis. 3rd ed., Verlag Chemie Deerfield Beach 1984; 6: 582-88.

d. Detection limit:

16 different mixtures of heparinized whole blood samples were used in the test. The mixtures were prepared to have the parameter levels indicated in the table below:

Target Concentrations of Test Sample Mixtures

Mix No.	K^+ mMol/L	Na^+ mMol/L	Cl^- mMol/L	Ca^{2+} mMol/L	Glu mMol/L	Lac mMol/L	tHb g/dL	pH pH	pO_2 mmHg	pCO_2 mmHg	Sat %	Bili µMol/L
1	8	120	98	1.99	3.15	5.04	15.598	7.538	493	10		5
2							15	7.58	545	10	100	
3	3.44	187.5	138	0.56	1.01	6.24	9.656	7.061	31.8	80		20
4	7						15	7.13	130	80	98	
5	2.26	191.7	144	0.57	2.61	2.97	15.503	6.892	22.5	150		0
6	7						15	7	15	150	10	
7	5.6	154.7	121	1.32	1.5	2.89	14.626	7.223	37.7	55.7		0
8	7						15	7.22	40	60	70	
9	4	183.4	133	0.42	2.25	9.01	4.481	7.499	198	26.9		48
10	7						15	7.36	230	30	100	
11	4	177.5	134	0.56	0.95	0.29	2.446	7.32	211	44		0
12	4	140	111	1.05	14.64	5.18	24.227	7.352	76.5	38.6		645
13	7	133.7	109	1.47	7.02	3.66	19.046	7.454	54.8	20		170
14	5.38	156.2	117	0.92	0.76	7.51	10.524	7.49	362	20		19
15	4	166.7	123	0.59	6.67	7.1	14.172	7.375	90.6	35.7		188
16	3.7	168.3	127	0.71	6.94	2.2	18.222	7.18	33.8	77.1		159

During a day of test, the levels of the parameters of each mixture drifted somewhat away from the initial level. However, this did not influence the quality of the study as each double measurement on an ABL8xx FLEX analyzer was complemented by corresponding measurements on the five ABL 735 analyzers. The concentrations of the measured mixtures represent the entire test/reportable range of all the parameters.

e. Analytical specificity:

pH/blood gas the following interference results are found for the pH and blood gas electrodes:

Substance	**Test Conc.**	**Interference on *p*O2 Electrode**
Halothane	3%	5 % increased sensitivity

Intralipid (20 % solution) in a concentration greater than 4 % (the final Intralipid level being 0.8 %) will give interference on pH measurements.

Electrolytes The following interference results are found for the electrolyte electrodes:

Substance Test Concentration		Interference on			
		cK^+ (4 mmol/L level)	cNa^+ (150 mmol/L level)	cCa^{2+} (1.25 mmol/L level)	cCl^- (110 mmol/L level)
Li^+	4 mmol/L	0	0	0	
K^+	12 mmol/L		-1	-0.01	
Na^+	100-180 mmol/L	0.1 to -0.1			
NH_4	1 mmol/L	0	0		
Ca^{2+}	5 mmol/L		0		
Mg^{2+}	5 mmol/L	0	0	0.05	
Br^-	10 mmol/L				41
F^-	1 mmol/L				0
I^-	3.0 mmol/L				30–90
ClO_4^-	1.5 mmol/L				8-30
HCO_3^-	25-50 mmol/L				0.1 mmol/L Cl^- per mmol/L HCO_3^-
Lactate	10 mmol/L				0
Acetyl-salicylic acid	3.0 mmol/L				2
Ascorbic acid	1.0 mmol/L				0
pH ≤ 7.2		0	0	0.01	-1
pH≥ 7.6		0	0	-0.01	1

Sulphide will give erroneously high cCl^- results.

Metabolites
The following interference results are found for the metabolite electrodes:

Substance	**Test Conc. (mmol/L)**	**Interference on**	
		cGlucose (4.0 mmol/L level)	cLactate (1.5 mmol/L level)
Acetylsalicylic acid	3	< 0.1	< 0.1
Ascorbic acid	2	< 0.1	< 0.1
Chlorpromazine HCl	0.2	< 0.1	< 0.1
Dopamine HCl	1.0	< 0.1	< 0.1
Ethanol	79	< 0.1	< 0.1
Salicylic acid	4	< 0.1	< 0.1
Ibuprofen	2	< 0.1	< 0.1
Thiocyanic acid	24	Interference	Interference
Paracentamol-4-acetamidopenol	2	< 0.1	< 0.1
Acetoacetic acid	2	< 0.1	< 0.1
Bilirubin (unconjugated)	0.34	< 0.1	< 0.1
Bilirubin (conjugated)	0.46	< 0.1	< 0.1
Creatinine	3	< 0.1	< 0.1
Urea	84	< 0.1	< 0.1
Uric acid	1.5	< 0.1	< 0.1
Lactic acid	12	< 0.1	
Pyruvate	2	< 0.1	< 0.1
Glycolic acid	1	< 0.1	Interference
D-glucose	67		<0.1
Citrate	50	-0.37	0.19
Oxalate	90	-0.47	0.14
Heparin	8000 IU/dL	< 0.1	< 0.1
EDTA	3	< 0.1	< 0.1
Fluoride	50	-0.36	<0.1
Maltose	13.3	0.75-4.2*	<0.1

cGlu level measure on Cal 1 (10 mmol/L) and Cal 2 (0 mmol/L)

Hematocrit %	ΔcLactate % at:	
	5 mmol/L	15 mmol/L
0	0.7 %	0.7 %
45	0.0 %	0.0 %
60	-0.5 %	-2.0 %
75	-2.2 %	-5.0 %

Oximetry Parameters

The substances against which the oximetry parameters (cHb, sO_2, FO_2Hb, FCOHb, FMetHb, FHHb, FHbF) and ctBil were tested for interference given in the table below:

(SAT100 blood reference test sample: ctHb = 15 g/dL, sO_2 = 100 %, FO_2Hb = 0.7%, FMetHb = 0.5 %, ctBil = 0, pH = 7.4. Parameters sensitivity from the influence on the absorbance spectrum from various substances.)

Substance	Test conc.	Change on							
		ctHb (g/dL)	sO_2 (%)	FO_2Hb (%)	FCOHb (%)	FMetHb (%)	FHHb (%)	FHbF (%)	ctBil (µmol/L)
Intralipid	4Vol % [e]	-0.5	0.1	-1.3	0.5	0.9	-0.1	11	0 4 [b]
Intralipid	2 Vol % [f]	-0.4	0.1	-0.3	0.3	0.1	-0.1	11	7 2 [b]
HbF [a, c]	20 %	-0.02	1.17	0.04	0.73	0.37	-1.14	0	-14
SHb	10 %	0	-1.0	0.9	-0.1	0.1	-0.9	Not Tested	
pH	7.1 7.9	-0.5 -0.6	-0.5 0.6	-0.2 -0.5	-0.4 1.0	0.1 0.1	0.5 -0.6	-19 13	0 -5
Cardio Green [c]	5 mg/L	-0.16	0.29	1.14	0.07	-0.93	-0.29	-5	-20
Evans Blue [c]	5 mg/L	-0.04	0.14	0.28	-0.20	-0.20	0.14	-5	5
Betacarotene in plasma [c]	3.7 µmol/L	0.0	-0.02	0.03	-0.01	-0.04	0.02	0.1	-0.2
Patent Blue [c]	10 mg/L	-0.16	0.39	0.86	-0.47	0.00	-0.38	-21	38
Methylene Blue [c]	30 mg/L	-0.7	-3.4	5.6	-3.0	-6.2	3.6	-37	-25
HiCN [c]	0.11 mmol/L	0.26	-1.5	-3.0	-0.5	0.5	1.5	24	47
MCHC [c, d] newborn range	320 g/L 350 g/L	No Interference							-12 17
Sedimentation rate	100 arb. Units	< ± 0.5	No Interference						Not Tested

Notes:

a) If function "Correction for HbF levels less than 20%" is activated, the change is 0 for all parameters.

b) Plasma sample.

c) Calculated value from mathematical superposition of measured pure interference spectrum on measured reference spectrum.

d) ctBil = 400 µmol/L

e) Intralipid (20 % solution) at 4 Vol % gives final test level of 0.8 %.

f) Intralipid (20 % solution) at 2 Vol % gives final test level of 0.4 %.

There is no interference from fetal hemoglobin (HbF when the analyzer applies HbF correction.

There is no interference from bilirubin (conjugated/unconjugated) up to 1000 µmol/L.

Known interfering substances
The following substances are known to affect or interfere with measurements on the ABL 800 FLEX analyzers.

Substance	Interference
Halothane (anesthetic)	May give unreliable pO_2 results.
Liquid therapy, protamine sulphate treatment	In OXI measurements. After measurement on blood from a patient who has received liquid therapy of protamine sulphate it may be necessary to clan the analyzer using the Cleaning program.
Methylene Blue HiCN (medication)	In Oxi measurements.
Anions: Br^-, I^-, S^{2-} and ClO^-_4 (drugs)	Erroneously high cCL^- results
Anticoagulant (sampling)	Anticoagulants that contain sodium salts will give erroneously high cNa^+ results. Sodium fluoride with or without EDTA and oxalate (di Na) influence cGlu results. Sodium fluoride gives erroneously high cNA^+ and low cCa^{2+}, cGlucose, and cLactate results. Tri sodium citrate influences cNA^+,cK^+ and cGlu results. Thus radiometer recommends the exclusive use of heparin as anticoagulant. Solutions containing organic preservatives may damage the ion-selective membranes of the K and Glu electrodes when introduced into the analyzer.
Thiocyanic Acid (degradation product from treatment with Nitroprusside. Also produced in thiosulphate treatment of cyanide poisoning)	Erroneously high cGlu and CLac measurements.
Glycolic Acid (ethylene glycol degradation product)	Erroneously high cLac measurements
Insufficiently stabilized blood. Caustic fluids (e.g. strong acids or bases, detergents, etc.). Fluids that precipitate. Fluids that affect the sensor enzymes. Fluids that form complexes with the	Other fluids mode allows you to measure on fluids other than heparinized human blood. **Warning/Caution**: Be aware that some substances, such as listed in the left column, measured in the Other fluids,

Substance	Interference
analyzer solutions (calcium). High viscosity fluids. Hydrophobic fluids. Reactive fluids.	mode may damage the instrument or the electrodes. This can affect the subsequent measurement on human blood or quality control solutions.
Carboxymethyl cellulose (CMC)	Some auto-venting arterial blood samplers contain carboxymethyl cellulose (CMC) in the porous vent. CMC can dissolve into the sample and give erroneously low cCa^{2+} results. Therefore we recommend Radiometer accessories together with our analyzers, e.g., PICO 70 arterial blood sampler which is specifically designed to minimize sample contamination with CMC.
Glucosamine	Interference on cGlu up to 1.06 mmol/L
Galactose, maltose, mannose, xylose	Interference – see Interference Tests in chapter 5 of the ABL800 FLEX Reference Manual.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

The sponsor completed a study to verify that the new analyzer ABL800 FLEX with FLEXQ Module performs substantially equivalent to the predicate device ABL800 FLEX. Several blood samples covering the entire measuring range of pH, pO_2, pCO_2, chloride, calcium, potassium, sodium, glucose, lactate, total hemoglobin, oxygen saturation and total bilirubin were prepared. The prepared blood samples were simultaneously measured on ABL800 FLEX analyzers with FLEXQ module using safe PICO samplers and on ABL800 FLEX using PICO70 samplers. The results of the study are shown below.

FLEXQ/safe PICO: ABL800 FLEX analyzer with FLEXQ module using safe PICO samplers.
ABL800 FLEX/PICO70: ABL800 FLEX using PICO70 samplers.

Analyte	Range	n	Slope	Intercept	Correlation Coefficient
pH	6.8-7.6	62	1.00483	-0.0337735	0.999867
pO_2 (mmHg)	0-600	56	0.973437	1.55976	0.999945
pCO_2 (mmHg)	0-180	63	0.987866	0.0132798	0.999095
Cl^-(mmol/L)	99-149	63	0.993333	0.565056	0.999218
Ca^{2+}(mmol/L)	0-2.4	63	0.974538	0.0261278	0.999881
K^+ (mmol/L)	2.5-8.5	55	1.00667	0.00350562	0.999316
Na^+ (mmol/L)	110-190	63	0.98835	0.850219	0.999893
Glu (mmol/L)	0-15	57	1.0098	-0.135106	0.999299
Lac (mmol/L)	0-15	63	1.01218	0.0671328	0.997542
tHb (g/dL)	0-25	63	0.999705	0.0582917	0.999891
sO_2 (%)	0-120	57	1.00182	-0.153404	0.999969
tBil (µmol/L)	0-500	44	1.02145	-1.17612	0.998849

b. Matrix comparison:

Not applicable. The ABL800 FLEX with FLEXQ modle is designed for use on undiluted whole human blood and expired air samples only.

3. Clinical studies:

a. Clinical Sensitivity:

Clinical studies are not typically submitted for this device type.

b. Clinical specificity:

Clinical studies are not typically submitted for this device type.

c. Other clinical supportive data (when a. and b. are not applicable):

4. Clinical cut-off:

Not applicable.

5. Expected values/Reference range:

The measuring range for a parameter is the range within which the analyzer is physically capable of measuring. The measuring range corresponds to the "range of indication" as defined in the "International vocabulary of basic and general terms in metrology" (VIM). The test range for a parameter is the range within which accuracy and precision of a measured parameter was specified and intended to lie within specified limits. The test range corresponds to the "measuring range" as defined in the "International vocabulary of basic and general terms in metrology (VIM).

The following measured parameters are available independent of analyzer configuration.

Expected values/Reference ranges cited from references. (see listed references below).

Blood

Parameter	Unit	Measuring Range	Test Range
pH	pH scale	6.300-8.000	7.0-7.7
cH^+	Mmol/L	10.0-501	20-100
pCO_2	mmHg; torr kPa	5.0-250 0.67-33.3	15-150 2.00-20.00
pO_2	mmHg; torr kPa	0.0-800 0.00-107	15-530 2-70
ctHb	g/dL g/L mmol/L	0.00-27.7 0.0-277 0.00-17.2	7-25 70-250 5-15
sO_2	% fraction	0-100* 0.0-1.000*	0-100 0-1
FO_2Hb	% fraction	0-100* 0.0-1.000*	0-100 0-1
FCOHb	% fraction	0-100* 0.0-1.000*	0-20 0.0-0.2
FMetHb	% fraction	0-100* 0.0-1.000*	0-20 0.0-0.2
FHHb	% fraction	0-100* 0.0-1.000*	0-100 0-1
FHbF	% fraction	0-100* 0.0-1.000*	0-80 0.0-0.8
cK^+	mmol/L; meq/L	0.5-25.0	2-8
cNa^+	mmol/L; meq/L	7-350	120-180
cCa^{2+}	mmol/L meq/L mg/dL	0.20-9.99 0.40-19.98 0.8-40.04	0.5-2.5 1.0-5.0 2.0-10.0
cCl^-	mmol/L; meq/L	7-350	85-140
cGlucose	mmol/L mg/dL	0.0-60 0-1081	2-15 36-270
cLactate	mmol/L; meq/L mg/dL	0.0-30 0-270	0.3-10 2.0-90
ctBil	µmol/L mg/dL mg/L	1-1000* 0.0-60.0* 0-600*	0-400 0-23.5 0-235

*The values are for the analyzer with the activated “Out of range suppression” function. In case this function has not been activated, the measuring range will be as follows:

Parameter	Unit	Measuring Range
sO_2 , FO_2Hb FCOHb, FMetHb	% fraction	-2.0 % to 102.0 % -0.020- to 1.020
FHbF	% fraction	-15 % to 102 % -0.15 to 1.02
ctBil	µmol/L mg/dL mg/L	-20 to 1000 -1.2 to 58.5 -12 to 585

Expired air

Parameter	Unit	Measuring Range	Test Range
pCO_2	mmHg kPa	5.0-250 0.67-33.3	15-150 2.00-20.00
pO_2	mmHg kPa	0.0-800 0.00-107	15-530 2-70

Baro

Parameter	Unit	Measuring Range	Test Range
P(amb)	mmHg; Torr kPa	450-800 60.0-106.7	450-800 60.0-106.7

Other fluids

All parameters available on your ABL800 FLEX analyzer can be measured on fluids other than heparinized human whole blood.

NOTE: Before using this mode you must establish "user-defined corrections" specified for the fluid in question. The corrections assume a linear correlation between the measured value and the reference instrument. The data used for establishing "user-defined corrections" have to cover the desired measuring range; an evaluation of the linearity within the range is necessary as well. If no use-defined corrections are entered, you will measure in this mode as if on heparinized whole human blood.

List of references

1. Kristensen HB, Salomon A, Kokholm G. International pH scales and certification of pH.

2. Definition of pH scales, standard reference values, measurement of pH and related terminology (Recommendations 1994). Pure and Appl Chem 1985; 57, 3: 531 - 42.

3. Burnett RW, Covington AK, Maas AHJ, Müller-Plathe O *et al*. J Clin Chem Clin Biochem 1989; 27: 403 - 08.

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Scand J Clin Lab Invest 1993; 53, Suppl 214: 84 - 94.

5. Glucose. NCCLS Publication RS1-A. Villanova, Pa: NCCLS, 1989.

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8. Kristoffersen K. An improved method for the estimation of small quantities of alkali-resistant hemoglobin in blood. Scand J Clin Lab Invest 1961; 13: 402.

9. Quantitative measurement of fetal hemoglobin using the alkali denaturation method. Approved Guideline. NCCLS Publication H13-A 1989; 9, 18.

10. Begmeyer. Methods of enzymatic analysis. 3rd ed., Verlag Chemie Deerfield Beach 1984; 6: 582-88.

N. Instrument Name:

ABL800 FLEX with FLEXQ Module

O. System Descriptions:

1. Modes of Operation:

   The ABL800 FLEX with FLEXQ is identical to the analyzer part of the ABL800 FLEX Analyzer (k041874). The FLEXQ allows the capability of automatic sampling from up to three blood samplers. The FLEXQ module is designed to work with the vented arterial blood sampler, safe PICO (k043143). The upgraded software controls all steps of the FLEXQ module and the ABL800 FLEX Analyzer. If required, manual introduction of a blood sample may be performed as well. This may be relevant when having only small sample volumes e.g. in capillary tubes, or if it becomes necessary to perform an urgent measurement when all three slots of the FLEXQ sample tray are occupied.

2. Software:

   The software is partly based on commercially available standard software such as Windows XP and SYBASE and partly on software developed in-house, the software interfaces via serial channel or Ethernet with TCP/IP to LIS HIS systems. The use of the XP platform provides the ABL800 FLEX with a user interface that is fully customizable.

   In addition to the features of the ABL800 FLEX software, the software of the ABL800 FLEXQ also has the capacity of controlling the functioning of the FLEXQ module.

Electrical Safety and EMC

Approvals:	UL, CSA. In compliance with IEC 61010-1. Installation category II
EMC Emission:	the equipment complies with the emission requirements for Class B equipment in EN 61326-1: Electrical equipment for measurement, control and laboratory use – EMC requirements part 1: General requirements.
EMC Immunity:	The equipment complies with immunity requirements in EN 61326-1: Electrical equipment for measurement, control and laboratory use – EMC requirements part 1: General requirements.

3. Specimen Identification:

   See specimen sampling and handling below.

4. Specimen Sampling and Handling:

   Once an arterial blood sample has been collected as prescribed with the safePICO sampler, the sampler is provided with the vented tip cap on the syringe luer tip and arranged in a free slot of the FLEXQ sampler tray. The presence of the sampler is detected and the barcode of the sampler is read out. The sampler is now put in queue to be analyzed. When the analyzer is ready to analyze the blood sample, the magnet system is activated to rotate and move the steel ball in the sampler for approximately 5 seconds to mix the sample. The sampler tray is then displaced to position the sampler in front of the inlet of the analyzer. The inlet probe of the analyzer penetrates the top of the tip cap and enters the sample barrel to aspirate the blood sample into the analyzer. The sampler is then analyzed and the sampler may be removed and discarded as prescribed.

5. Calibration:

   The two calibration solutions, the rinse solution, the cleaning solution, the tHb calibrator and the calibration gases for the pO_2 and pCO_2 sensors are of the same formulations utilized in the ABL800 FLEX Analyzer 510(k) 041874.

6. Quality Control:

See Traceability, Stability, Expected values (controls, calibrators, or methods) indicated above.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In the "Performance Characteristics" Section above:

The following Software Review of this device was presented by the sponsor and reviewed:

- Level of Concern
- Software Description
- Device Hazard Analysis
- Software Requirements Specification (SRS)
- Architecture Design Chart
- Design Specification
- Traceability Analysis
- Development
- Validation, Verification and Testing (VV&T)
- Revision Level History
- Unresolved anomalies (bugs)
- Release Version Number

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.